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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,080	09/24/2001	Mathias Uhlen	2039.000	9697

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EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 04/28/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,080

Applicant(s)

UHLEN ET AL.

Examiner

Jon D Epperson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-26 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other:

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DETAILED ACTION

Please Note: In an effort to enhance communication with our customers and reduce processing time, Group 1627 is running a Fax Response Pilot for Written Restriction Requirements. A dedicated Fax machine is in place to receive your responses. The fax number is (703) 308-4315. A fax cover sheet is attached to this Office Action for your convenience. We encourage your participation in this Pilot program. If you have any questions or suggestions please contact Andrew Wang, Supervisory Patent Examiner, at (703) 306-3217. Thank you in advance for allowing us to enhance our customer service. Please limit the use of this dedicated Fax number to responses to Written Restrictions.

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to **Group Art Unit 1639**.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372. This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

2. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

- I. Claims 1, 8 (in part), 9-13 (in part), 14, 17, 18, 19 are drawn to a method for affinity separation wherein the affinity ligand is an immobilized proteinaceous ligand wherein one or more of its asparagines has been modified.

- II. Claim 2, 9-13 (in part) are drawn to a method of stabilizing an affinity ligand by modifying one or more of its asparagines.
- III. Claims 3, 5, 9-13 (in part) are drawn to a method of preparing a combinatorial library of protein molecules wherein the protein has one or more of its asparagines modified before randomization.
- IV. Claims 4, 8 (in part), 9-13 (in part), 15-16 are drawn to a method of phage display wherein a protein expressed on the phage surface has had one or more of its asparagines modified.
- V. Claim 6, 9-13 (in part), 19, 22, 23 and 24 are drawn to a product described as a combinatorial protein wherein one or more of said proteins asparagines have been modified before a randomization step.
- VI. Claims 7, 9-13 (in part) and 21 are drawn to a product described as a "fusion protein" comprising a first part wherein one or more naturally occurring Asparagines have been modified and a second part being a randomized protein molecule.
- VII. Claims 25-26 are drawn to a product described as a nucleic acid molecule encoding a protein from Groups I-VI above and the host cell expressing the protein encoded by the nucleic acid molecule.

3. The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the reasons that follow.

4. PCT Rule 13.2 states that unity of invention shall be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.” It further defines “special technical feature” as “those technical features that define a contribution which each of the claimed inventions, claimed as a whole, makes over the prior art.”

5. First, a special technical feature does not link the methods of Groups I-IV. The methods do not share a special technical feature because they use different steps, require different reagents and/or will produce different results. In the instant case, Group IV requires method steps for “phage display”, which are not steps that would be required by the methods of Groups I-III i.e., the methods of Groups I-IV do not necessarily have anything in common. Likewise, Group I requires method steps for “affinity separation and use of a proteinaceous affinity ligand”, which are steps that are not required by the methods of Groups II-IV i.e., the methods of Groups I-IV do not necessarily have anything in common. Finally, Group III requires “method of stabilizing an affinity ligand”, which are method steps that are not required by the methods of Groups I-II and IV because the “affinity ligand” does not necessarily have to be a protein i.e., the methods of Groups I-IV do not necessarily have anything in common. Therefore, Groups I-IV do not share a special technical feature.

6. Furthermore, a special technical feature does not link the products of Groups V-VII. The products do not share a special technical feature because they differ in respect to their properties,

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their use and the synthetic methodology for making them. For example, Group VII is drawn to a “a nucleic acid molecule encoding a protein and a host cell expressing said nucleic acid”, which requires different reagents and/or materials that are not required by Groups V-VI i.e., nucleic acid and host cell. Likewise, Group VI is drawn to a “fusion protein”, which requires different reagents and/or materials than Groups V and VII i.e., Groups V and VII do not necessarily require fusion proteins. Therefore, Groups V-VII do not share a special technical feature.

7. Finally, the technical feature linking groups V, II and I appears to be that they represent product, process specially adapted for the manufacture of said product, and a method for the use of said product, respectively, wherein said product is a combinatorial protein that has one or more of its asparagine residues modified.

8. However, Friedman et al (Friedman, A. R.; Ichhpurani, A. K.; Brown, D. M.; Hillman, R. M.; Krabill, L. F.; Martin, R. A.; Zurcher-Neely, H.A.; Guido, D. M. “Degradation of growth hormone releasing factor analogs in neutral aqueous solution is related to deamidation of asparagine residues” 1991, Int. J. Peptide Protein Res. 37, 1991, 14-20), teaches combinatorial proteins that have their asparagine residues replaced (i.e., modified) by serine residues (see Friedman et al, page 15, column 1, paragraph 3; see also page 18, column 2).

9. Therefore, the technical feature linking the inventions of groups I, II and V does not constitute a species technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

10. Accordingly, groups I-VII are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

11. Finally, see 37 CFR § 1.475 - Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage, cited in part below (especially sections (c) and (d)).

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression special technical features shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

A product and a process specially adapted for the manufacture of said product;
or
A product and process of use of said product; or
A product, a process specially adapted for the manufacture of the said product,
and a use of the said product; or
A process and an apparatus or means specifically designed for carrying out the
said process; or
A product, a process specially adapted for the manufacture of the said product,
and an apparatus or means specifically designed for carrying out the said
process.

(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.

(d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

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12. Groups V, II and I represent product, process specially adapted for the manufacture of said product, and a use of the said product of use, respectively (see above, parts b and d).

However, the technical feature that links the claims (combinatorial protein wherein one or more of said proteins asparagines have been modified before a randomization step i.e., the product) is known in the art, as set forth above. Thus, the instant claims lack unity of invention.

Species Election

13. This application contains claims directed to more than one species of the generic invention for Groups I-VI. These species are deemed to lack unity of invention because they are not so linked to form a single general inventive concept under PCT Rule 13.1.

14. If applicant elects any of the inventions of Groups I-VIII applicant is required to elect from the following patentably distinct species. Claims 1, 2, 3, 4, 6 and 7 are generic to Groups I, II, III, IV, V and VI, respectively. Applicant must elect 1 species from each subgroup below.

Subgroup 1: Species of amino acid (e.g., see claim 13)

Applicant must elect for the purposes of search a single species of amino acid e.g., lysine, aspartic acid or leucine.

Subgroup 2: Species of protein (e.g., see claims 19, 20)

Applicant must elect, for the purposes of search, a single species of protein e.g., albumin-binding protein (ABD). Please do not elect a general class of proteins like "enzyme" because more than one species of protein would then be erroneously elected i.e., pick 1

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"one" protein (see specification for specific examples). Please make sure to indicate all of the parts of a "fusion" protein in the event that a fusion protein is elected.

15. In addition, if applicant elects the inventions of Groups VII applicant is required to elect from the following additional patentably distinct species.

Subgroup 3: Species of host cell (e.g., see claim 26)

Applicant must elect for the purposes of search a single species of host cell (see specification for examples).

16. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons.

17. PCT Rule 13.2 states that unity of invention shall be fulfilled when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features". It further defines "special technical feature" as "those technical features that define a contribution which each of the claimed inventions, claimed as a whole, makes over the prior art". For example, unity of invention is fulfilled if:

- (a) all alternatives have a common property; **and**
- (b) (i) a common structure is present, i. e. a significant structural element is shared by all alternatives, or
- (b) (ii) in cases where the common structure can not be the unifying criterion, all alternatives belong to a recognized class of compounds in the art to which the invention pertains. (MPEP 1850).

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18. In the instant case, the amino acids in subgroup 1 do not have a common property or common structure. Likewise, the proteins in subgroup 2 do not have a common property or common structure.

For these reasons, election under these rules is proper and required.

19. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

20. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

21. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

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22. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143). Because the above restriction/election requirement is complex, a telephone call to applicants to request an oral election was not made. See MPEP § 812.01.

23. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

24. Applicant is also reminded that a 1 - month (not less than 30 days) shortened statutory period will be set for response when a written requirement is made without an action on the merits. This period may be extended under the provisions of 37 CFR 1.136(a). Such action will not be an "action on the merits" for purposes of the second action final program, see MPEP 809.02(a).

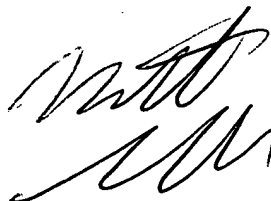
25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached Monday through Friday from 8:30 to 4:30 p.m..

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26. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
April 21, 2003

BENNETT GEL SA
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'JDE', written over the printed name of the examiner.